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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/506,766	11/12/2004	Pascal Bigey	029440.00001	3543

4372 7590 06/13/2007

ARENT FOX PLLC
1050 CONNECTICUT AVENUE, N.W.
SUITE 400
WASHINGTON, DC 20036

EXAMINER	
SHIN, DANA H	

ART UNIT	PAPER NUMBER
1635	

MAIL DATE	DELIVERY MODE
06/13/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/506,766	BIGEY ET AL.	
	Examiner	Art Unit	
	Dana Shin	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *13 April 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-3,7-16,29 and 30* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3,7-16,29 and 30* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *12 November 2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of Application/Amendment/Claims

This Office action is in response to the communications filed on April 13, 2007.

Currently, claims 1-3, 7-16, and 29-30 are pending. Applicants have cancelled claims 4-6 and 17-28 and added claim 30. The newly added claim, claim 30, reads on the elected invention and will therefore be examined on the merits.

The following rejections are either newly applied or are reiterated and are the only rejections and/or objections presently applied to the instant application.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Response to Arguments and Amendments

Withdrawn Rejections

Any rejections not repeated in this Office action are hereby withdrawn.

New Rejections

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-3, 7-16, and 29-30 are rejected under 35 U.S.C. 103(a) as being unpatentable over Szyf et al. (WO 99/24583, applicant's citation No. A01) in view of Monia et al. (US 6,008,048) and Deeley et al. (US 6,001,563).

The claims are drawn to a combination product comprising at least one MBD2 antisense oligonucleotide and bleomycin, wherein the antisense oligonucleotide is administered about 30 minutes after the injection of the bleomycin, and wherein the antisense oligonucleotide is targeted to SEQ ID NO:1.

Szyf et al. teach SEQ ID NO:5, which is identical to instantly claimed SEQ ID NO:1. They teach that demethylase inhibitors can be used as anticancer agents and the demethylase inhibitors include antisense oligonucleotides or ribozymes targeted to the demethylase cDNA sequence comprising SEQ ID NO:5 (pages 5-7). See also claims 3 and 13. They teach that cancer cells express high level of DNA demethylase and DNA demethylase activity is observed in several cancer cell lines (page 41). They teach that a vector expressing the human demethylase cDNA in the antisense orientation reduces tumorigenesis in cells *in vitro* (page 43). Szyf et al. do

not teach a combination product comprising a demethylase antisense oligonucleotide and bleomycin, nor do they teach a method of delivering the combination product.

Monia et al. teach pharmaceutical compositions comprising one or more antisense oligonucleotides and one or more chemotherapeutic agents including bleomycin (column 24, lines 4-10). They teach that the antisense oligonucleotides and chemotherapeutic agents can be used simultaneously or sequentially (column 24, lines 28-29). They teach the formulation of therapeutic compositions and their subsequent administration via various routes is within the skill of those in the art (column 24, lines 38-63). They teach that pharmaceutical compositions comprising antisense oligonucleotides can be formulated in various ways and that the techniques of making pharmaceutical compositions are well known in the pharmaceutical industry (columns 11-12).

Deeley et al. teach that antisense oligonucleotides can be produced from an expression vector in cells (column 14, lines 53-65; columns 15-17 and 28). They teach that the expression vector containing an antisense oligonucleotide can be introduced into mammalian cells by various means including electroporation and microinjection (column 17, lines 26-34). They also teach pharmaceutical compositions suitable for injectable use (column 24).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to combine the antisense oligonucleotide targeted to SEQ ID NO:5 of Szyf et al. with a chemotherapeutic agent bleomycin of Monia et al. and to express the antisense oligonucleotide of Szyf et al. from an expression vector for electroporation or microinjection as taught by Deeley et al.

One of ordinary skill in the art would have been motivated to combine the teachings of the prior art with a reasonable expectation of success because the full length target gene cDNA sequence (MBD2 or demethylase) was known in the art, which is disclosed as SEQ ID NO:5 in the Szyf et al's reference, and because MBD2 was known to be overexpressed in several cancer cells and therefore reducing the expression of MBD2 by virtue of antisense oligonucleotides was suggested to reduce tumorigenesis by Szyf et al. (pages 41, 43). Furthermore, a combination product comprising one or more antisense oligonucleotides and one or more chemotherapeutic agents, administered either together or separately, was known to be used as anticancer agent in the art as taught by Monia et al. (column 24). Since Szyf et al. expressly teach that an anti-MBD2 antisense oligonucleotide can be an anticancer agent (pages 5-7), and since a combination product comprising antisense oligonucleotides and chemotherapeutic agents was known in the art as of the earliest filing date sought in the instant application, one of ordinary skill in the art would have been motivated to combine the antisense anticancer agent targeted to the instantly claimed SEQ ID NO:1 as taught by Szyf et al. with one or more chemotherapeutic agents for additive or synergistic effect of reducing tumorigenesis. Moreover, the skilled artisan would have been motivated to construct a vector that expresses the anti-MBD2 antisense oligonucleotide with a reasonable expectation of success because Deeley et al. teach that antisense oligonucleotides can be produced from an expression vector in mammalian cells and that vectors comprising antisense oligonucleotides can be introduced into mammalian cells via electroporation or microinjection. Since various pharmaceutical formulations comprising antisense oligonucleotides and the techniques of making pharmaceutical compositions were well known in the pharmaceutical industry at the time the invention was made, as taught by Monia et

al. (columns 11-12), one of ordinary skill in the art would have had a reasonable expectation of success in optimizing the delivery conditions for the MBD2 antisense oligonucleotide thereby arriving at the instantly claimed combination product for anticancer treatment.

See also *In re Kerkhoven*, wherein the court expressed the following:

"It is *prima facie* obvious to combine two compositions each of which is taught by the prior art to be useful for the same purpose, in order to form a third composition to be used for the very same purpose...[T]he idea of combining them flows logically from their having been individually taught in the prior art." *In re Kerkhoven* 626 F.2d 846, 850, 205 USPQ 1069, 1072 (CCPA 1980).

Since both antisense and bleomycin were recognized in the art as anticancer therapeutic agents, it would have been prima facie obvious to combine them for treatment of cancer with a reasonable expectation of success. See also MPEP 2144.06.

Accordingly, the instantly claimed invention taken as a whole would have been *prima facie* obvious at the time of filing.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Dana Shin whose telephone number is 571-272-8008. The examiner can normally be reached on Monday through Friday, from 8am-4:30pm EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Douglas Schultz can be reached on 571-272-0763. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Dana Shin
Examiner
Art Unit 1635

/J. E. Angell/
Primary Examiner
Art Unit 1635